REMARKS/ARGUMENT

An interview was held with the Examiner and reported in the Examiner's Interview Summary on December 1, 2010. It was stated in the Summary that the difference between the instantly claimed PS composition and that of the prior art was discussed. Also discussed was a possible product by process claim to different instant product from prior art. Further, it was discussed that a possible declaration could show the instant method of making results in a materially different product that the prior art.

To this end Applicants have amended main Claim 58 to define the composition of matter of the instant invention in terms consistent with the discussion at the interview. As amended, Claim 58 recites more particularly, that the phosphatidylserine composition of matter is for use as a dietary supplement, nutraceutical food and/or drug additive, and that the PS divalent metal ion salt is in powder form, that its level is from about 1 to about 45% (w/w), that it is dispersed in the oil base, and that it is enzymatically prepared from in a substantially aqueous system, from lecithin which is not solubilized in the reaction system in the presence of a phospholipase. Support for the amendments may be found, for example, in Example 1.

Claims 1-57, 59, 61, 63, 66, 67, 68 and 76 are cancelled without prejudice. The remaining claims are amended consistent with claim 58. It is respectfully submitted that no new matter has been added.

The amendment of claim 58 is predicated on proofs that there is in fact a difference between the instantly claimed PS composition and that of the prior art. This difference is made evident in claim 58 by the recitation of a product by process limitation that shows the different instant product produce and how it differs from prior art. Further, the proofs that show the invention of claim 58 are contained in two declarations submitted herewith that unequivocally show that the claimed method of making the PS composition is, in

fact, a materially different product that the prior art cited and applied. The two declarations submitted herewith comprise a declaration by Neta Scheinman, attached hereto is marked Exhibit B, and a declaration by Gai Ben-Dror, attached hereto marked Exhibit A; both are inventors of the inventions claimed.

As detailed in the Gai Ben-Dror declaration, (Exhibit A), attached hereto, PS salts which are prepared in a diphasic system are soluble in oils. As shown in the Gai Ben-Dror declaration, PS salts prepared in various diphasic systems, such as those of De Ferra et al. gave clear solutions when mixed with oils, i.e. were soluble in the oil. Dispersions of such salts in oil could not be prepared, due to their solubility in the oil.

As detailed in the Neta Scheinman declaration, the storage stability of PS salts in accordance with the invention, which are prepared in an aqueous system, contained in capsules, was tested for storage stability under mild (ambient) and extreme (accelerated) conditions (Part 1). In addition, the storage stability of PS salts in accordance with the invention was compared with the storage stability of commercially available PS (by Manufacturer A), claimed to be "stable" (Part 2 and Figure 2).

As shown in the Neta Scheinman declaration, (Exhibit B), the PS composition of matter as defined in claim 58, contained in gel capsules, exhibited long storage stability under mild (ambient) and extreme (accelerated) conditions. Remarkably, the PS in accordance with the invention contained in capsules, did not degrade even after 12 months of storage at extreme conditions, and 24 months at ambient, normal storage conditions, and was more stable than the commercially available PS.

The principle reference cited of record is De Ferra et al. which explicitly teaches the preparation of PS, and its purification by crystallization as the calcium salt, in a diphasic system using as starting material lecithin, which was dissolved in the organic phase. As explained in the interview, PS calcium salts produced in diphasic systems from lecithin

dissolved in the organic phase, such as those taught by De Ferra, are soluble in oils. The proof of this evidential fact is the attached Declaration by inventor Gai Ben-Dror, Exhibit A. Example 2 of De Ferra et al. was repeated. The product and MCT (an oil) were dissolved in hexane and concentrated under vacuum to give a **clear** PS fluid, proving that the PS is soluble in oil. The additional examples in the Declaration, all further demonstrate that producing PS in a diphasic reaction, where the starting material lecithin is dissolved in the organic phase, results in a PS that is soluble in oil. Thus the product of the prior art is different from the product of the invention wherein the PS composition of matter of the invention, which is prepared in an aqueous system from non-solubilized lecithin. The resulting product is different in that it is in the form of a divalent metal salt in powder form, that is insoluble in and is dispersed in an edible oil. Not soluble in the oil. This is a major inventive difference, which highly influences the stability of the PS.

Explanations appear in the Gai Ben-Dror declaration, (Exhibit A), regarding the basis of this difference. This system employed by the present invention uses non-solubilized lecithin as the starting material for making the PS, and does not contain any significant amounts of organic solvents. The system is characterized by being substantially aqueous, and by employing non-solubilized lecithin as the substrate of the enzymatic reaction between the lecithin and the added serine. Since lecithin is rather sticky, the reaction of lecithin with the serine may be facilitated by the addition of small quantities of organic solvent before initiating the enzymatic reaction. This feature is optional, and may be used for improving the contact between lecithin and serine and assist the dispersion of the lecithin in the reaction mixture, without solubilizing (dissolving) the lecithin in the reaction system. This option of adding a small amount of an organic solvent to the reaction system before the addition of lecithin is mentioned in Example 1 of the patent application as strictly an optional feature. This option is absent, for example, from the synthetic procedure described in the Neta Scheinman declaration (Exhibit B).

As further stated in the Ben-Dror declaration, it is believed that the differences between the product of the presently claimed invention and the PS product described in De Ferra *et al.* (EP 922707) may be explained as follows:

"*Although the phosphatidylserines (PS's) in both cases are in the form of their salt with a divalent ion, their solubility characteristics are different. The difference in solubility characteristics is believed to result from the fact that PS can arrange in different forms of molecule groups, according to the reaction medium in which it was produced. In De Ferra et al., during the reaction, the lecithin starting material is dissolved in a non-polar organic solvent, and it is believed that the phospholipids tend to form micelles where their non-polar side (the fatty acids "tails") turn toward the surrounding medium (the non-polar organic solvent in this case). In contrast, in the subject invention, during the mono-phasic reaction in water, which is a polar medium, the lecithin is not solubilized and it is believed that the phospholipids form the opposite arrangement, and turn their polar head group (the "phosphoserine") outside, toward the medium (which is water, i.e. polar), while their fatty acid tails (non-polar) turn away from the medium. Those two forms of arrangement of the molecules in the formed PS are believed to be retained after the PS is isolated. This explanation is believed to clarify the different solubility characteristics of PS in oil, which is a non-polar medium. PS that was produced from lecithin in an organic solvent, by bi-phasic reaction, has a form of a "non-polar arrangement", where the fatty acids tails are turned to the outer side of the micelles, i.e. toward the medium. When PS with a "non-polar arrangement" is mixed with oil, which is non-polar, it will be dissolved in the oil and thus form a solution. This is the case with De Ferra et al.*

On the other hand, a PS that was produced from lecithin in a water system, by mono-phasic aqueous reaction, has a form of a "polar arrangement", where the fatty acids tails are turned to the inner side of the micelles, and the polar side of the PS is turned outwards, i.e. toward the medium. When PS with a "polar arrangement" is mixed with oil, which is non-polar, it will be "rejected" by the non-polar oil and therefore will not be soluble in the oil. This PS "polar arrangement"

will form a dispersion, rather than a solution in oil. This is the case with the PS of the present invention." See illustration in the Ben-Dror Declaration.

Further, as proven by the Neta Scheinman declaration, (Exhibit B), the present inventive product is considerably more stable over longer storage than prior art products consisting of conventional solutions of PS.

In light of the foregoing remarks, and the submission of evidence proving the inventive difference between the present inventive product of claim 58 and the prior art cited and applied, it is respectfully urged that the application be reconsidered and that the presently amended claims should be favorably considered as placing the application in condition for allowance. Early passage of this case to issue is earnestly solicited.
If any questions remain, a telephone call would be appreciated.

It is respectfully requested that, if necessary to effect a timely response, this paper be considered as a Petition for an Extension of Time, time sufficient, to effect a timely response, and shortages in this or other fees, be charged, or any overpayment in fees be credited, to the Deposit Account of the undersigned, Account No. 500601 (Docket no. 7056-X08-020).

Respectfully submitted,

Martin Fleit

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Attached: Declarations of Gai Ben-Dror (Exhibit A); Neta Scheinman (Exhibit B)